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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,026	03/16/2000	Michael D. West	000270-111	1630

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/527,026	West et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 14, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, ar* 9 and 198-231 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, and 198* (9) 231 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Mar 16, 2000* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) ✓
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This an original application filed March 16, 2000, which claims benefit to provisional applications; 60/179,486, filed February 1, 2000, and 60/152,340, filed September 7, 1999.

Applicants amendment filed November 14, 2002, paper number 17, has been received and entered. Claims 83, 93-112, 119, 147, 166, 181-193 and 197 have been canceled. Claims 69, 113, 128, 132, 136 and 151 have been amended. Claims 69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, 198-231 are pending and currently under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: It was not executed in accordance with either 37 CFR 1.66 or 1.68. Specifically, the specification was filed with a preliminary amendment and an unexecuted declaration. A signed declaration was filed May 28, 2002, paper number 14, however the declaration did not specifically refer to the preliminary amendment (see top of front page of the declaration). A substitute declaration or oath to correct the deficiencies clearly indicating the application serial number and indicating 'as amended in the preliminary amendment filed March 31, 2000' is required. See MPEP 604.08.

Claim Objections

Claim 69, 113, 128, 132, 136 and 151 objected to because the claims included internal periods is withdrawn.

Amending the claim to include parenthesis instead of periods has obviated the basis of the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, 198-231 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of providing primary cells comprising: a) enucleating an oocyte of a first mammalian species and transferring the nucleus of a primary cell from the same species as the recipient oocyte into said oocyte; b) activating the NT unit; c) culturing the activated NT unit in a immunocomprimized mouse to produce a teratoma; and d) isolating a differentiated cell from said teratoma, and cells derived by said method, does not reasonably provide enablement for use

of any source of host cell from a first species, nor the use of any organism besides a mammalian species is withdrawn.

Amendments to the claims reciting and encompassing that the genetic material and oocyte are of the same species has obviated the basis of the rejection. With respect to limitations of forming a teratoma in mammals other than SCID mice, it is noted that the specification provides the guidance to practice this step only in SCID mice. However, upon review of the examples in the art for forming teratomas in mammals other than mice, Examiner acknowledges that this method step was practiced in other mammals at the time of filing. Further, upon review of the cited references and the art in general for forming teratomas, there is no evidence that the teratoma formed in SCID mice are any different than those formed in other mammals. Therefore, Examiner agrees with Applicants' arguments that the step encompassing the formation of teratoma should not be limited to formation in SCID mice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, 198-231 stand rejected under 35 U.S.C. 102(a/e) as being anticipated by Strelchenko *et al.* (US Patent 6,011,197) or Damiani *et al.* (US Patent 6,258,988) as evidenced by Shiels *et al.* (Nature 399:316-317) and Betts *et al.* (PNAS 98:1077-1082).

First, Applicants note the specific terms recited in the claims, specifically the use of 'a senescent or near-senescent donor mammalian cell or the nuclei or chromosomes of said cell' and that the method results in rejuvenated cells with increased EPC-1 and telomerase activity. Second, Applicants summarize the teachings of Strelchenko *et al.* and Damiani *et al.* noting that neither reference specifically states to use senescent or near-senescent cells as donor cells or that the resulting methods result in a rejuvenated cell. Citing a reference not used in the basis of the rejection, Shiels *et al.*, Applicants argue that the art teaches away from the instantly claimed invention because the telomeres of cloned sheep are as short as the telomeres of the donor cell (as evidenced by the first cloned sheep Dolly). Applicants argue that Strelchenko *et al.* and Damiani *et al.* teach using quiescent cells in nuclear transfer protocols, not senescent or near-senescent cells, and that the methods taught by Strelchenko *et al.* and Damiani *et al.* would not result in rejuvenated cells with increased telomere length as compared to the donor. See Applicants'

amendment filed November 14, 2002, paper number 12, pages 7-8. Applicants' arguments have been fully considered but not found persuasive.

Initially, it is noted that the claims encompass the embodiments for the use of nuclei and chromosomes, and the teachings of Strelchenko *et al.* and Dimiani *et al.* anticipate these embodiments because while cells may differ in phenotypic characteristics, proliferating, quiescent or senescent, the nuclear donor material encompassed by nuclei and chromosomes is structurally a DNA molecule. Isolating the nuclear donor material, either a nuclei or chromosomes, from any cell type for use in nuclear transfer methodology would not convey to the donor material the characteristics of the cell from which it was isolated. Therefore, the source of the nuclei or chromosome used in the method would be indistinguishable whether isolated from proliferating, quiescent or senescent cells. Further, while proliferating, quiescent and senescent cells can be distinguished by phenotypic characteristics displayed by the cells, the nuclear material of each of these cells, i.e. the chromosomes, would be the same for each of the proliferating, quiescent or senescent cells. When used in the methods of nuclear transfer nuclear transfer to an oocyte results in the reprogramming of the nuclear material, the nucleus and/or chromosomes, absent other cellular material would be the same as the nucleus and chromosomes as used in Strelchenko *et al.* and Dimiani *et al.* and would inherently result in the same rejuvenated cell. Therefore, the teachings of Strelchenko *et al.* and Dimiani *et al.* for the use of a nucleus and/or chromosomes in nuclear transfer techniques anticipates the instant claims.

With respect to arguments regarding the use of different cells, it is noted that Strelchenko *et al.* and Dimiani *et al.* teach that any primary cell can be used in the nuclear transfer methodology. For example, Strelchenko *et al.* teaches that the cell can be obtained from any part of the animal and can be 'a differentiated cell', 'a hepatic cell', or 'a neuronal cell' (bridging columns 6-7) each of which represents cells comprising terminally differentiated cells which would be considered senescent because they no longer proliferate. Therefore, the specific cells contemplated by Strelchenko *et al.* and Dimiani *et al.* comprise the use of senescent cells, and thus, implicitly anticipate the claims for the use of senescent cells. As noted in the previous office action, the method of nuclear transfer inherently results in a rejuvenated cell, in particular since the primary donor cell has a limited capacity of cell doubling in culture and a primary cell does not have the capacity to result in an embryo capable of generating a complete cloned animal. Further, transplanting a primary cell does not result in the formation of a teratoma from which cell types from each of the three germ layers can be identified. Applicants' arguments are based in part on the unexpected observation that nuclear transfer results in a cell with increased telomere length, however there is no argument to the fact that the present invention relies on art enabled embodiments of nuclear transfer and that the methods as instantly claimed provide no novel steps not disclosed in Strelchenko *et al.* or Dimiani *et al.* With respect to the unexpected result, Examiner acknowledges that nuclear transfer methods using a sheep primary donor cell and sheep oocyte results in a sheep whose cells have shorter telomeres than an aged matched wild type sheep. However, while using nuclear transfer methods in sheep resulted in the first

cloned sheep Dolly having shorter telomeres than aged matched wild type sheep subsequent work by Shiels *et al.* (Nature 399:316-317) indicate that this was more related to the cell used to generate Dolly. Shiels *et al.* teach that subsequent cloned sheep derived from different cells resulted in cloned sheep with telomeres that were statistically indistinguishable from aged matched wild type sheep (see final paragraph and figure 1). The expression of EPC-1 was not characterized by Shiels *et al.*, however because the reprogramming of the nuclear donor by nuclear transfer increased telomere length, it would be expected that the EPC-1 gene expression would be affected in a similar manner as an inherent property of reprogramming by nuclear transfer methodology. With respect to other mammals, the present specification bases it unexpected results on experiments using a bovine nuclear donor and oocyte. Betts *et al.* teaches that in unlike sheep, cows cloned using nuclear transfer methods result cloned offspring which had increased telomerase activity and restored telomere length (see results summarized in abstract). Betts *et al.* acknowledge the observations made in Dolly, however teach that nuclear transfer methodology in cattle results in reprogramming of telomerase activity in the developing embryo and results in restored telomere length in the resulting cloned cattle (see final paragraph). Applicants arguments that the present invention encompasses surprising and unexpected results is not convincing because the unexpected result is inherent to practicing nuclear transfer in cattle. Further, with respect to other mammals, telomere size of resulting animals appears to be related to the donor cell used in the nuclear transfer methods as demonstrated by Shiels *et al.* Applicants arguments that the present invention encompasses unexpected results and that the art

teaches away from these unexpected results is unconvincing because the specification relies on the nuclear transfer methods taught in the art at the time of filing and as discussed above the art teaches that unexpected results relied upon are inherent to specific species of mammal or donor cell used. Because the specification relies on the nuclear transfer methods taught in the art, the present specification and claims are subject to the same limitations and inherent results of these nuclear transfer methods.

Both, Strelchenko *et al.* and Dimiani *et al.* teach that the methodology can be used to generate an animal in which a heterologous sequence is introduced. The specification relies on the methods taught in the art for the practice of the claimed invention, and the instant claims recite the same method steps known in the art of nuclear transfer, and thus practicing the methods known in the art as taught by Strelchenko *et al.* and Dimiani *et al.* would inherently result in cells with the observed phenotype. The instant claims are not distinguished from nuclear transfer methods known in the art by simply providing a new description of the resulting product or reciting a new intended use in the preamble of claim which encompasses methodology previously disclosed in the art. As noted in the previous office action, when, the claimed and prior art methods are identical or substantially identical, or products are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its

fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, the instantly claimed methods and the resulting cells from said methods are materially the same as would be used and made by the methods of nuclear transfer known and taught in the art, and thus, the methods taught in Strelchenko *et al.* and Dimiani *et al.*, only that the result of practicing the method would result in a cell with a phenotype not previously described. Thus, the methods taught in Strelchenko *et al.* and Dimiani *et al.* anticipate the instantly claimed methods and cells produced by said method.

Claims 69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, 198-231 are rejected under 35 U.S.C. 102(b) as being anticipated by Robl *et al.* (WO 98/07841) as evidenced by Shiels *et al.* (Nature 399:316-317) and Betts *et al.* (PNAS 98:1077-1082).

Applicants argue that Robl *et al.* does not disclose resulting cells with increased telomere length, and as argued above for Strelchenko *et al.* and Dimiani *et al.* does not anticipate the instantly claimed invention. See Applicants' amendment filed November 14, 2002, paper number 17, page 9. Applicants' arguments have been fully considered but not found persuasive.

As summarized in the previous office action, Robl *et al.* teach a method of nuclear transfer wherein the resulting cell is chimeric cell comprising an enucleated oocyte which is different from that of the transferred nuclei. As argued above, because the specification relies on

the methods taught in the art for the practice of the claimed invention, and since practicing the method of nuclear transfer would inherently result in the cells presently claimed, the methods and resulting cells taught in Robl *et al.* anticipate the claims as they are drawn to generating a modified cell. As evidenced by Shiels *et al.* sheep cloned subsequent to Dolly derived from different cells resulted in cloned sheep with telomeres that were statistically indistinguishable from aged matched wild type sheep (see final paragraph and figure 1). With respect to other mammals, like the examples provided and relied upon for unexpected results, Betts *et al.* teaches that in unlike sheep, cows cloned using nuclear transfer methods result cloned offspring which had increased telomerase activity and restored telomere length (see results summarized in abstract). Betts *et al.* acknowledge the observations made in Dolly, however teach that nuclear transfer methodology in cattle results in reprogramming of telomerase activity in the developing embryo and results in restored telomere length in the resulting cloned cattle (see final paragraph). Applicants arguments that the present invention encompasses surprising and unexpected results is not convincing because the unexpected result is inherent to practicing nuclear transfer in cattle. Further, with respect to other mammals, telomere size of resulting animals appears to be related to the donor cell used in the nuclear transfer methods as demonstrated by Shiels *et al.* Applicants arguments that the present invention encompasses unexpected results and that the art teaches away from these unexpected results is unconvincing because the specification relies on the nuclear transfer methods taught in the art at the time of filing and as discussed above the art teaches that unexpected results relied upon are inherent to specific species of mammal or donor

cell used. Because the specification relies on the nuclear transfer methods taught in the art, the present specification and claims are subject to the same limitations and inherent results of these nuclear transfer methods. Since the claimed and prior art methods are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Further, whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, the instantly claimed methods and the resulting cells from said methods are materially the same as would be used and made by the methods of nuclear transfer known and taught in the art, and thus, the methods taught in Robl *et al.* anticipate the instantly claimed methods and cells produced by said method.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, 198-231 stand provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 87-210 of copending Application No. 09/250,879.

Claims 69-82, 84-92, 113-118, 120-146, 148-165, 167-180, 194-196, 198-231 stand provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 69-231 of copending Application No. 09/656,173.

Applicants acknowledge the double patenting rejection and request that the rejection be held in abeyance until an allowance is negotiated. Applicants affirm that a terminal disclaimer

will be submitted in the instant application once allowable subject matter has been indicated. See Applicants' amendment, pages 9-10.

Applicants' arguments have been fully considered, however the rejection can not be held in abeyance. The claims of the instant application and the pending claims of 09/250,879 and 09/656,173 are drawn to the same invention, each drawn to a method of generating a rejuvenated cell through nuclear transfer techniques.

References which are relevant to the instant application but not relied upon in the instant office action:

Lanza *et al.* Science 288:665-669, represents post-filing art disclosing results of cloning cattle which is similar to that in the working examples of the present specification.

Cibelli *et al.* Science 280:1256-1258, teaches that at the time of filing that nonquiescent primary fibroblasts of a cow were used in nuclear transfer methods to produce cloned calves. Further, Cibelli *et al.* teaches that the use of a cell from cell line CL1 which was 0.8 population doubling from senescence produced a cloned embryo which developed into a fetus, and that the resulting fetal cells from the cloned fetus demonstrated properties similar to fetal cells obtained from an age matched non-manipulated fetus (see page 1258, first column). The work of Cibelli *et al.* demonstrates that at the time of filing that donor cells, both non-quiescent or near-senescent cells primary cells, were used in nuclear transfer methods and resulted in rejuvenated cells capable of forming a fetus and cloned calves.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
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